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ORIGINAL ARTICLE

SHOULD ITERATIVE CYTOREDUCTIVE SURGERY AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY BE CONSIDERED THE BEST TREATMENT OF RECURRENT PSEUDOMYXOMA PERITONEI (PMP)?

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ABSTRACT: *Background and objectives*. After CRS-HIPEC, approximately 25-45% of patients with pseudomyxoma peritonei (PMP) experience recurrence even after optimal treatment. Treatment of recurrent PMP is controversial and based mainly on surgeon and center experience. The aim of this study was to assess the feasibility, safety, and oncological benefit of iterative CRS-HIPEC (i-CRS-HIPEC) in patients with recurrent PMP.
Methods. Consecutive PMP patients treated according to an institutionally standardized protocol of CRS-HIPEC were retrospectively analyzed for postoperative and long-term oncological outcomes.
Results. Between January 2010 and May 2023, 76 patients with PMP were treated with CRS and HIPEC. Of these, 21 patients underwent i-CRS-HIPEC for recurrent PMP and were compared with those who underwent primary surgery (p-CRS-HIPEC). Peritoneal Cancer Index (PCI), cytoreduction grade (CC), and histological grade (acellular mucin, low-grade, and high-grade PMP) didn't differ significantly from primary CRS-HIPEC. Postoperative outcomes and complications were similar between the groups. After a median follow-up of 24.5 months (IQR 18.89-30.18), there was no difference between groups in the 5-year OS and DFS.
Conclusions. i-CRS-HIPEC can be performed safely and is associated with the same oncological outcome in terms of local disease control and should be considered the first choice for recurrent PMP after appropriate patient selection.

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IMPACT STATEMENT: The treatment of recurrent pseudomyxoma peritonei PMP is controversial and based mainly on surgeon and center experience. In this study, we have assessed the impact of iterative CRS-HIPEC (i-CRS-HIPEC) in terms feasibility, safety, and oncological benefit in recurrent PMP.

Key Words: *peritoneal neoplasms; cytoreductive surgery; HIPEC, appendiceal tumors.*

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BACKGROUND

Pseudomyxoma peritonei (PMP) is a rare malignant clinical syndrome with an estimated incidence of 2-4 cases per million people per year (1-3) and is clinically characterized by implantation of neoplastic cells on peritoneal surfaces with progressive mucin production (mucinous ascites) throughout the abdominal cavity. PMP was first described by Werth in 1884 as the peritoneal spread of an ovarian neoplasm (4);

however, recent evidence has shown that PMP most commonly results from the spread of mucin-producing cells from an appendiceal neoplasm or, in a minority of cases, from mucinous extra-appendiceal neoplasms (5-7).

Cytoreductive surgery (CRS) combined with hyperthermic intraperitoneal chemotherapy (HIPEC) has significantly improved oncological outcomes in selected patients with PMP. The rationale of CRS-HIPEC is to remove all macroscopic peritoneal implants by multiple peritonectomies and surgical resections and to treat microscopic residual tumors with hyperthermic intraperitoneal chemotherapy (8). CRS-HIPEC has been included in several international and national guidelines as the standard of care for PMP (9) and is the only treatment with a potential chance of cure and long-term disease control for affected patients (10-11).

Although management and overall survival have recently improved, approximately 25-45% of patients with PMP experience recurrence even after receiving optimal combination treatment (12-15). The options available range from repeated surgery with or without HIPEC to palliative systemic chemotherapy, and the clinical management of recurrence is not yet standardized (16).

The main aim of this study was to assess the feasibility, safety, and oncological benefit of i-CRS-HIPEC in terms of local control and survival in patients with recurrent PMP.

METHODS

Study design and data collection

This study is a retrospective and comparative analysis of patients with primary or recurrent PMP who underwent CRS with HIPEC between January 2010 and May 2023 at the Surgical Oncology department of the Veneto Institute of Oncology IOV-IRCCS. After written consensus, all patients were selected and treated according to an institutionally standardized protocol; prior to surgery, eligibility for CRS and HIPEC was reviewed by our multidisciplinary tumor board, considering clinical and pathological features and imaging results (CT scan, PET-CT scan or abdominal MRI in doubtful cases). The study was approved by the institute's ethics committee (BIOPMP CET ANV: 2024-08) and in accordance with the Helsinki Declaration of 1975, as revised in 1983.

Patients

Patient records were extracted from our institutional electronic health record software and prospectively collected in an electronic database. All patients were informed of the nature of the procedure and signed an informed consent form. Demographic and preoperative data included age, sex, body mass index (BMI), ECOG performance status, comorbidities according to the ASA physical status classification system, and systemic chemotherapy before or after CRS-HIPEC.

Intraoperative and postoperative short-term outcome variables

Intraoperative variables collected included operative time, blood loss, and number of packed red blood cells (PRBCs) transfused. Abdominal spread of the tumor was assessed intraoperatively using the Peritoneal Cancer Index (PCI), and residual disease after CRS was classified according to the Completeness of Cytoreduction (CC) score (17); surgical technique (open, video-laparoscopic, or hybrid approach) and HIPEC technique (open or closed) were recorded, as well as the number and type of peritonectomies and organ resections. The surgical procedure consisted of peritonectomy and cytoreductive surgery as described by Sugarbaker (8). The HIPEC protocol consisted of cisplatin at 90mg/m^2 plus mitomycin-C 12 mg/m^2 at a target temperature of 41.5°C maintained for 60 minutes at a target flow rate of approximately 1000 ml/min. Histology of the PMP was performed in all cases according to the PSOGI histological classification (18). All specimens obtained from outside institutions were systematically reviewed. Postoperative data included Intensive Care Unit (ICU) length of stay, hospital length of stay, 30-day readmission rate, and complications. Complications were graded according to the Clavien-Dindo grading system (19). All patients underwent an institutionally approved follow-up schedule with at least clinical examination, CT scan, and serum tumor markers every six months for the first three years and then every 12 months up to 10 years postoperatively.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics for Mac v.29.0.1.0 (IBM Corporation, Armonk, NY, USA). Patients were divided into two main groups: patients who underwent i-CRS-HIPEC and the control group consisting of patients who underwent primary cytoreductive surgery and HIPEC (p-CRS-HIPEC). Quantitative data are presented as median

and interquartile range (IQR), and categorical data are presented as numbers and percentages. Categorical data and quantitative data were analyzed using chi-squared or Fisher's exact test and t-test, respectively. Median overall survival (OS) and disease-free survival (DFS) were calculated using the Kaplan-Meier estimator. Statistical significance was considered when p-values were less than 0.05. DFS and OS were calculated from the day of CRS-HIPEC.

RESULTS

Between January 2010 and May 2023, 80 patients with PMP were referred to our institution; 76 patients were selected and treated with CRS and HIPEC. Two patients were excluded at presentation and underwent palliative surgery only, and two other patients were excluded at recurrence for unresectable disease. Three of these unresectable patients died within 12 months after diagnosis. Twenty-one patients underwent i-CRS-HIPEC, of which 15 and 6 patients underwent a second and a third i-CRS-HIPEC, respectively. A comparison of demographic and preoperative variables (**Table 1**, **Table 2**) showed that the BMI was significantly lower in the i-CRS-HIPEC group (20.96 *vs.* 25.95, p = .012) and that a greater percentage of i-CRS-HIPEC patients received neoadjuvant chemotherapy within six months prior to CRS-HIPEC (28.6% *vs.* 3.6%, p = .005), while there was no difference between the two groups for neoadjuvant chemotherapy treatment beyond six months prior to surgery and for adjuvant chemotherapy treatment. When comparing the intraoperative variables (**Table 3**, **Table 4**), PCI was higher in the p-CRS-HIPEC patients (21 *vs.* 15, p = .072), although not statistically significant. Correspondingly, the extent of surgery was lower in the i-CRS-HIPEC group, as evi-

Table 1. *Comparison of demographic and preoperative variables between First CRS-HIPEC and Iterative CRS-HIPEC.*

	P-CRS-HIPEC N = 56	I-CRS-HIPEC N = 21	P
Age at diagnosis (y), median (IQR)	52 (47 - 63)	52 (44 - 65)	0.861
Gender, n (%)			
Male	18 (32.7%)	5 (23.8%)	0.580
Female	37 (67.3%)	16 (76.2 %)	
BMI (kg/m²), median (IQR)	25.95 (22.14 - 28.73)	20.96 (19.58 - 26.97)	**0.012**
ASA physical status, n (%)			
ASA 1	6 (10.9%)	1 (4.8%)	
ASA 2	33 (60%)	17 (81%)	0.226
ASA 3	16 (29.1%)	3 (14.3%)	
Performance status, n (%)			
ECOG 0	50 (90.9%)	16 (76.2%)	
ECOG 1	4 (7.3 %)	5 (23.8%)	0.142
ECOG 2	1 (1.8%)	0 (0.0%)	
PMP Histology, n (%)			
Acellular Mucin	8 (14.5%)	1 (4.8%)	0.289
Low-grade PMP	35 (63.6%)	14 (66.7%)	
High-grade PMP	8 (14.5%)	6 (28.6%)	
High-grade PMP with SRC	4 (7.3%)	0 (0%)	
Systemic chemotherapy, n (%)			
SC <6 months before intervention	2 (3.6%)	6 (28.6%)	**0.005**
SC >6 months before intervention	6 (10.9%)	1 (4.8%)	0.666
SC after intervention	1 (1.8%)	0 (0%)	0.534
Months from last CRS-HIPEC, median (IQR)	-	22.67 (16.67 - 39.10)	-

Abbreviations. CRS, Cytoreductive Surgery; HIPEC, Hyperthermic Intraperitoneal Chemotherapy; IQR, Interquartile Range; BMI, Body Mass Index; ASA, American Society of Anesthesiologists; ECOG, Eastern Cooperative Oncology Group; PMP, Pseudomyxoma Peritonei; SRC, Signet Ring Cells; SC, Systemic Chemotherapy.

Table 2. *Comparison of demographic and pre-operative variables between first i-CRS-HIPEC and second i-CRS-HIPEC.*

	FIRST I-CRS-HIPEC N = 15	SECOND I-CRS-HIPEC N = 6	*P*
Age at diagnosis (y), median (IQR)	52 (44 - 72)	51 (41 - 55)	0.308
Gender, n (%)			
Male	4 (26.7%)	1 (16.7%)	0.613
Female	11 (73.3%)	5 (83.3%)	
BMI (kg/m²), median (IQR)	20.63 (19.34 - 26.01)	25.13 (19.43 - 29.36)	0.218
ASA physical status, n (%)			
ASA 1	1 (6.7%)	0 (0.0%)	0.662
ASA 2	11 (73.3%)	6 (100%)	
ASA 3	3 (20.0%)	0 (0.0%)	
Performance status, n (%)			
ECOG 0	11 (73.3%)	5 (83.3%)	0.573
ECOG 1	4 (26.7%)	1 (16.7%)	
ECOG 2	0 (0.0%)	0 (0.0%)	
PMP Histology, n (%)			
Acellular Mucin	0 (0.0%)	1 (16.7%)	0.624
Low-grade PMP	10 (66.7%)	4 (66.7%)	
High-grade PMP	5 (33.3%)	1 (16.7%)	
High-grade PMP with SRC	0 (0.0%)	0 (0.0%)	
Systemic chemotherapy, n (%)			
SC <6 months before intervention	4 (26.7%)	2 (33.3%)	0.300
SC >6 months before intervention	0 (0.0%)	1 (16.7%)	0.613
SC after intervention	0 (0.0%)	0 (0.0%)	-
Months from last CRS-HIPEC, median (IQR)	24 (16 - 37)	25 (18 - 57)	0.425

Abbreviations: CRS, Cytoreductive Surgery; HIPEC, Hyperthermic Intraperitoneal Chemotherapy; IQR, Interquartile Range; BMI, Body Mass Index; ASA, American Society of Anesthesiologists; ECOG, Eastern Cooperative Oncology Group; PMP, Pseudomyxoma Peritonei; SRC, Signet Ring Cells; SC, Systemic Chemotherapy.

denced by the shorter duration (555 *vs.* 605 minutes, p = .011), lower number of peritonectomies and visceral resections (1 *vs.* 3 p = <.001), (1 *vs.* 3, p = <.001), and lower median blood loss (20.96 *vs.* 25.95, cc, p = .012). Major complications requiring surgical intervention were observed in 4 patients (19.0%) in the i-CRS-HIPEC group compared with 12 patients (21.8%) in the p-CRS-HIPEC cohort. In the i-CRS-HIPEC group, these complications included two anastomotic leaks, one postoperative bleeding event, and one bowel perforation (**Table 5**).

The histology of PMP did not show a statistically significant difference between the two groups (p = .289); however, a higher percentage of acellular mucin cases were found in the first treatment group (14.5% *vs.* 4.8%), while a greater proportion of high-grade PMP was found in the patients with recurrence (28.6% *vs.* 14.5%), as expected. After a median follow-up of 24.53 months (18.89-30.18), the 5-year OS and DFS were 94.9.0% and 44.5%, respectively. There was no significant statistical difference in 5-year overall survival (OS) and disease-free survival (DFS) between the two groups, 93.1% and 46.6% for p-CRS-HIPEC and 100% and 41.7% for i-CRS-HIPEC, respectively (**Figure 1**).

DISCUSSION

Despite recent improvements in management and survival outcomes, approximately 25-45% of patients with PMP experience recurrence even after optimal treatment (12-15). The clinical management of recurrence is not standardized and the options available can range from non-operative management, including the watch-and-wait strategy, to palliative systemic chemotherapy and iterative surgery with or without the addition of HIPEC. The potential survival bene-

Table 3. *Comparison of intraoperative and postoperative variables between First CRS-HIPEC and Iterative CRS-HIPEC.*

	P-CRS-HIPEC N = 56	I-CRS-HIPEC N = 21	P
Intraoperative PCI, median (IQR)	21 (13 - 28)	15 (11 - 19)	0.072
CC score, n (%)			
CC0	49 (89.1%)	15 (71.4%)	
CC1	6 (10.9%)	5 (23.8%)	0.087
CC2	0 (0.0%)	1 (4.8%)	
Surgical technique, n (%)			
Open	49 (89.1%)	20 (95.2%)	
Lap	5 (9.1%)	1 (4.8%)	0.668
Lap/Open	1 (1.8%)	0 (0%)	
HIPEC technique, n (%)			
Open technique	11 (20%)	4 (19%)	0.926
Closed technique	44 (80%)	17 (81%)	
Operation duration (min), median (IQR)	605 (480 - 720)	555 (497 - 585)	**0.011**
CRS variables			
Peritonectomies, median (IQR)	3.0 (2.0 - 4.0)	1.0 (0.0 - 1.5)	**<0.001**
Visceral resections, median (IQR)	4.0 (3.0 - 6.0)	1.0 (1.0 - 2.5)	**<0.001**
Bowel resections, n (%)	30 (54.5%)	11 (52.4%)	0.866
Stoma, n (%)	4 (7.3%)	1 (4.8%)	0.693
Blood loss (mL), median (IQR)	300 (100 - 575)	150 (100 - 375)	**0.012**
Blood transfusion			
Intraoperative transfusion, n (%)	17 (51%)	3 (23.1%)	0.329
Number of PRBCs, median (IQR)	0.0 (0.0 - 1.5)	0.0 (0.0 - 0.5)	0.226
Length of stay, (days), median (IQR)			
ICU length of stay	1.0 (1.0 - 2.0)	1.0 (1.0 - 2.0)	0.166
Hospital length of stay	11.0 (8.0 - 19.0)	11.0 (8.0 - 18.5)	0.726
Surgical complications*, n (%)			
Grade I-II	20 (36.4%)	7 (33.3%)	0.805
Grade III-IV	19 (34.5%)	4 (19.0%)	0.266
Reintervention, n (%)	12 (21.8%)	4 (19.0%)	0.791
Re-admission in 30 days, n (%)	2 (3.6%)	0 (0%)	0.376
90-day mortality, n (%)	0 (0%)	0 (0%)	-

**According to the Clavien-Dindo classification.*

Abbreviations. CRS, Cytoreductive Surgery; HIPEC, Hyperthermic Intraperitoneal Chemotherapy; IQR, Interquartile Range; PCI, Peritoneal Cancer Index; CC, Completeness of Cytoreduction; Lap, Laparoscopy; PRBCs, Packed Red Blood Cells; ICU, Intensive Care Unit.

fits of i-CRS-HIPEC in terms of feasibility, safety and oncological outcomes are not well established (16). Our study has clearly shown that iterative CRS and HIPEC is safe and effective in patients with recurrent disease with similar survival and disease control to patients treated for primary PMP. All the postoperative outcomes parameters including morbidity, length of stay, readmission rate and mortality are similar after i-CRS-HIPEC in comparison with p-CRS-HIPEC, confirming the safety of iterative procedures in recurrent PMP. Moreover, from an oncological point of view, i-CRS-HIPEC can offer durable disease control comparable to p-CRS-HIPEC. The study clearly showed that surgery should be always considered as the first line of treatment in every recurrent PMP even in patients with second recurrence. In this perspective the role of center expertise in patient selection is crucial. The preoperative multidisciplinary discussion should be focused on an accurate radiological evaluation to quantify disease burden and the possibility of achieving complete cytoreduction, with the final aim to maximize

Table 4. *Comparison of intraoperative and postoperative variables between first i-CRS-HIPEC and second i-CRS-HIPEC.*

	FIRST I-CRS-HIPEC N = 15	SECOND I-CRS-HIPEC N = 6	P
Intraoperative PCI, median (IQR)	18.50 (13.75 - 21.25)	6.00 (3.75 - 12.00)	**0.001**
CC score, n (%)			
CC0	10 (66.6%)	5 (83.3%)	0.643
CC1	4 (26.7%)	1 (16.7%)	
CC2	1 (6.7%)	0 (0%)	
Surgical technique, n (%)			
Open	15 (100%)	5 (83.3%)	
Lap	0 (0%)	1 (16.7%)	0.300
Lap/Open	0 (0%)	0 (0%)	
HIPEC technique, n (%)			
Open technique	2 (13.3%)	2 (33.3%)	0.549
Closed technique	13 (85.7%)	4 (66.7%)	
Operation duration (min), median (IQR)	567 (532 - 632)	472 (407 - 546)	**0.010**
CRS variables			
Peritonectomies, median (IQR)	1.0 (0.0 - 2.2)	0.0 (0.0 - 1.0)	0.110
Visceral resections, median (IQR)	1.5 (1.0 - 3.0)	1.0 (0.0 - 2.5)	0.424
Bowel resections, n (%)	10 (71.4%)	1 (16.7%)	0.050
Stoma, n (%)	0 (0%)	1 (16.7%)	0.300
Blood loss (mL), median (IQR)	200 (100 - 437)	125 (62 - 487)	0.922
Blood transfusion			
Intraoperative transfusion, n (%)	3 (20.0%)	0 (0%)	0.491
Number of PRBCs, median (IQR)	0.00 (0.00 - 1.75)	0.00 (0.00 - 0.00)	0.095
Length of stay, (days), median (IQR)			
ICU length of stay	1.00 (1.00 - 2.00)	1.00 (0.75 - 2.50)	0.882
Hospital length of stay	10.5 (8.0 - 21.0)	12.5 (6.5 - 23.0)	0.905
Surgical complications*, n (%)			
Grade I-II	6 (40.0%)	1 (16.7%)	0.254
Grade III-IV	3 (20.0%)	1 (16.7%)	0.807
Reintervention, n (%)	3 (20.0%)	1 (16.7%)	0.807
Re-admission in 30 days, n (%)	0 (0%)	0 (0%)	-
90-day mortality, n (%)	0 (0%)	0 (0%)	-

**According to the Clavien-Dindo classification.*

Abbreviations. CRS, Cytoreductive Surgery; HIPEC, Hyperthermic Intraperitoneal Chemotherapy; IQR, Interquartile Range; PCI, Peritoneal Cancer Index; CC, Completeness of Cytoreduction; Lap, Laparoscopy; PRBCs, Packed Red Blood Cells; ICU, Intensive Care Unit.

Table 5. *Major postoperative complications following p-CRS-HIPEC and i-CRS-HIPEC.*

	P-CRS-HIPEC N = 56	I-CRS-HIPEC N = 21
Perforation (IIIb*), n (%)	3 (5.4%)	1 (4.8%)
Anastomotic leak (IIIb*), n (%)	3 (5.4%)	2 (9.5%)
Hemoperitoneum (IIIb*), n (%)	6 (10.9%)	1 (4.8%)
Bleeding (IIIa*), n (%)	1 (1.8%)	0 (0.0%)
Abdominal fluid collection (IIIa*), n (%)	6 (10.9%)	0 (0.0%)

**According to the Clavien-Dindo classification.*

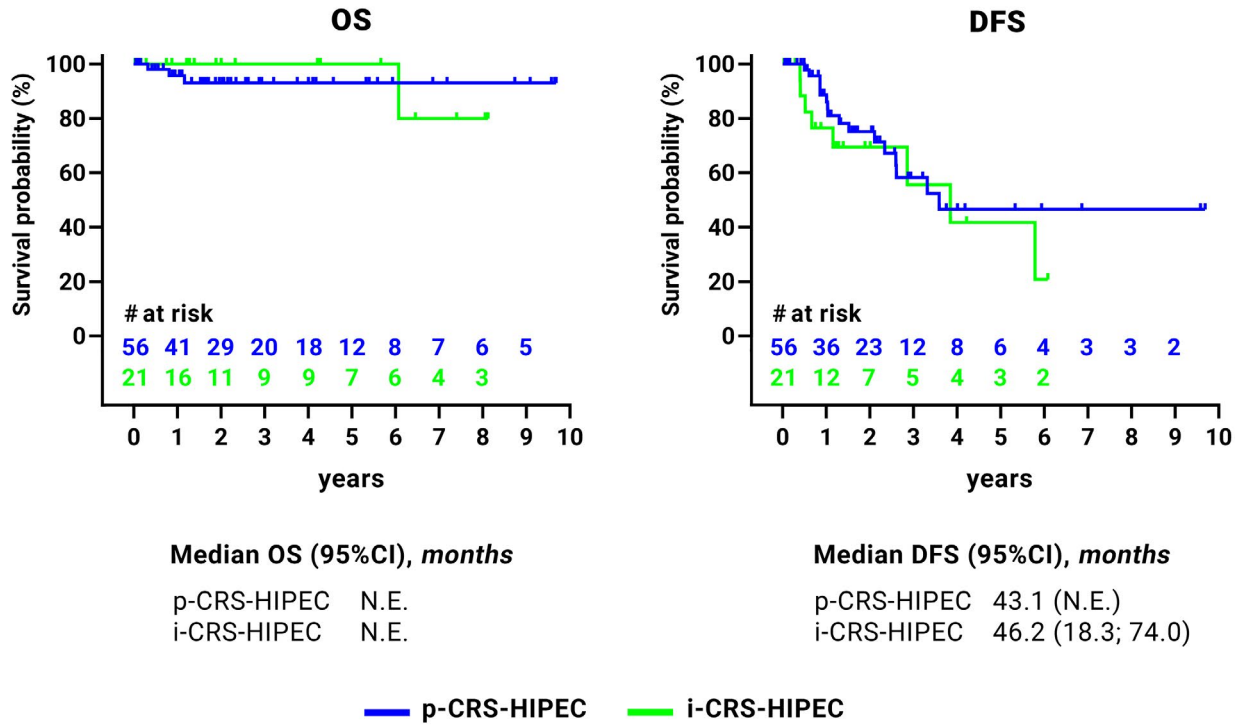

Figure 1. *Overall survival (OS) and disease-free survival (DFS) analysis.*

the benefit of surgery and reduce the risk of morbidity and mortality.

In our study the morbidity profile of CRS-HIPEC is lower to that reported in the literature for the surgical management of PMP (16). In the largest worldwide series, accounting for 1548 PMP patients treated with CRS-HIPEC, the rate of grade 3-5 complications, re-intervention and 90-day mortality is 32.7%, 9.2% and 3.1% respectively (9). We found comparable rates of severe complications, re-intervention, 30-day readmission and 90-day mortality rate between the i-CRS-HIPEC and p-CRS-HIPEC groups, confirming the safety and feasibility of i-CRS-HIPEC in patients with recurrent PMP (**Table 2**). I-CRS-HIPEC appears to be less surgically demanding, as evidenced by a significantly shorter operative time compared to p-CRS-HIPECs (p = .011). This result may be partly due to a lower disease burden in recurrent PMP, expressed by a lower median PCI (15 *vs.* 21) and a reduced need for peritonectomy and visceral resection. Although i-CRS-HIPEC appears to be less invasive, the grade 3-4 complication rate does not differ significantly from that of primary surgery (p = 0.266) with no 30-day mortality in both groups. This may be due, at least in part, to the fact that these patients had already undergone extensive surgery during p-CRS-HIPEC, which may have added complexity due to more adhesions and previous resections.

Our study further confirms that the comprehensive strategy of cytoreductive surgery and HIPEC provides good disease control of PMP both in the upfront treatment and recurrence setting, with excellent 5-year overall survival (OS) results. Specifically, only 4 out of 76 (5.26%) patients who underwent CRS and HIPEC for PMP at our institution died from causes unrelated to the oncological disease. In addition, patients who underwent i-CRS-HIPEC for recurrent PMP had a similar overall survival (OS) and disease-free survival (DFS) at 5 years as patients who underwent p-CRS-HIPEC (**Figure 1**). I-CRS-HIPEC guarantees the same disease control as p-CRS-HIPEC, confirming the favorable long-term survival outcomes observed in other studies of patients with PMP recurrence treated with i-CRS-HIPEC (14, 16, 24, 25).

The histological grading of PMP is considered an important piece of information in the selection process for evaluating all available treatment options. Our survival outcomes support the findings of previous studies regarding the more aggressive nature of high-grade PMP, but also the equivocal behavior of some cases of low-grade PMP with a certain tendency to recur (20-22). The appropriate identi-

fication of low-grade PMP patients at risk of recurrence may be improved in the future by using the Ki67 proliferation index or NGS analysis, and further studies are needed to validate this approach (23). PMP histologic grade (low/grade) does not appear to influence our clinical decision to treat recurrent patients with surgery. As expected, high-grade PMP showed a higher tendency to recur as shown by the higher percentage of high-grade PMPs seen in the i-CRS-HIPEC group (28.6% *vs.* 14.5%). Conversely, a slightly higher percentage of i-CRS-HIPEC patients received neoadjuvant chemotherapy in the six months prior to surgery (p = .005). This data confirms that the main selection criteria adopted for selecting the patient for i-CRS-HIPEC was the possibility to achieve a complete cytoreduction regardless of the histologic grade. Indeed, almost all (95%) of patients selected for i-CRS-HIPEC had a completeness of cytoreduction (CC) of 0-1, confirming the value of our patient selection process. Previous studies have confirmed our results in recurrent PMP, with a reported median progression free survival (PFS) in low-grade and high-grade PMP of 174.1 and 42.0 months respectively (24, 25). Recurrent high grade PMP with signet ring cells (SRC) is associated with a bad prognosis after i-CRS-HIPEC, with a reported PFS of 15 months only (25). In our study no PMP patient with high-grade SRC histology has been selected for i-CRS-HIPEC and should be therefore considered a relative contraindication for treatment.

The study has some limitations. In a retrospective analysis, the decision-making process and the selection criteria (clinical, radiological and histological) which might have driven the decision for i-CRS-HIPEC are difficult to identify. Early recurrence (within 12 months after p-CRS-HIPEC), symptomatic patients and unfavorable tumor biology (adenocarcinoma/signet ring histology) have been reported as factors associated with worse overall survival (26). The agreement on when and which recurrent patients are to select for i-CRS-HIPEC remains still controversial and there is no clear evidence supporting the decision. In our series the only criteria adopted was the possibility to achieve a complete or near complete cytoreduction and this decision to perform i-CRS-HIPEC was probably mainly based on this key factor. Moreover, the number of recurrent patients treated with i-CRS-HIPEC is to small for further sub analysis, such as investigate whether preoperative chemotherapy or histological grade could increase postoperative morbidity.

Another limit is the number of cases in the iterative group (n = 21), which may have limited some statistical analyses. In this perspective a multicentre data collection would in the next future strengthen the results of our study. In addition, it was not possible to retrospectively analyze postoperative pain and the impact of i-CRS-HIPEC on quality of life due to the lack of standardized recording in medical records. Finally, the potential role of biomolecular markers for prognostic stratification was not investigated and should be better defined in the next future.

CONCLUSIONS

Our study showed that i-CRS-HIPEC can be safely performed in recurrent PMP with proper patient selection and is associated with the same oncological outcome in terms of local disease control compared to primary treatment. Further strategies with new drugs and better patient selection for surgery are warranted in recurrent PMP in the coming years.

COMPLIANCE WITH ETHICAL STANDARDS

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Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Availability of data and materials

The data underlying this article are available in the public domain.

Publications ethics

Plagiarism

The article provides a comprehensive review of the latest studies in the field, with accurate citations.

Data falsification and fabrication

The writing and contents of the article are entirely original and were developed entirely by the authors.

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